

Environmental Suitability of *Vibrio* Infections in a Warming Climate: An Early Warning System

Jan C. Semenza,¹ Joaquín Trinanes,^{2,3,4} Wolfgang Lohr,^{5,6} Bertrand Sudre,⁷ Margareta Löfdahl,⁸ Jaime Martinez-Urtaza,^{9,10} Gordon L. Nichols,^{11,12,13} and Joacim Rocklöv^{5,6}

¹Scientific Assessment Section, European Centre for Disease Prevention and Control, Stockholm, Sweden

²Instituto de Investigaciones Tecnológicas, Universidade de Santiago de Compostela, Santiago, Spain

³Physical Oceanography Division, Atlantic Oceanographic and Meteorological Laboratory, National Oceanic and Atmospheric Administration, Miami, Florida, USA

⁴Cooperative Institute for Marine and Atmospheric Studies, Rosenstiel School of Marine and Atmospheric Sciences, University of Miami, Miami, Florida, USA

⁵Umeå Centre for Global Health Research, Umeå University, Umeå, Sweden

⁶Department of Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå University, Umeå, Sweden

⁷Epidemic Intelligence and Response, European Centre for Disease Prevention and Control, Stockholm, Sweden

⁸Folkhälsomyndigheten, Stockholm, Sweden

⁹The Milner Centre for Evolution, Department of Biology and Biochemistry, University of Bath, Bath, UK

¹⁰The Centre for Environment, Fisheries and Aquaculture Science (CEFAS), Weymouth, UK

¹¹Public Health England, London, UK

¹²University of Exeter, Exeter, UK

¹³University of East Anglia, Norwich, UK

BACKGROUND: Some *Vibrio* spp. are pathogenic and ubiquitous in marine waters with low to moderate salinity and thrive with elevated sea surface temperature (SST).

OBJECTIVES: Our objective was to monitor and project the suitability of marine conditions for *Vibrio* infections under climate change scenarios.

METHODS: The European Centre for Disease Prevention and Control (ECDC) developed a platform (the ECDC *Vibrio* Map Viewer) to monitor the environmental suitability of coastal waters for *Vibrio* spp. using remotely sensed SST and salinity. A case-crossover study of Swedish cases was conducted to ascertain the relationship between SST and *Vibrio* infection through a conditional logistic regression. Climate change projections for *Vibrio* infections were developed for Representative Concentration Pathway (RCP) 4.5 and RCP 8.5.

RESULTS: The ECDC *Vibrio* Map Viewer detected environmentally suitable areas for *Vibrio* spp. in the Baltic Sea in July 2014 that were accompanied by a spike in cases and one death in Sweden. The estimated exposure–response relationship for *Vibrio* infections at a threshold of 16°C revealed a relative risk (RR) = 1.14 (95% CI: 1.02, 1.27; $p = 0.024$) for a lag of 2 wk; the estimated risk increased successively beyond this SST threshold. Climate change projections for SST under the RCP 4.5 and RCP 8.5 scenarios indicate a marked upward trend during the summer months and an increase in the relative risk of these infections in the coming decades.

CONCLUSIONS: This platform can serve as an early warning system as the risk of further *Vibrio* infections increases in the 21st century due to climate change. <https://doi.org/10.1289/EHP2198>

Introduction

Vibrio spp. are aquatic bacteria that are ubiquitous in warm estuarine and coastal waters with low to moderate salinity (Vezzulli et al. 2013). *Vibrio cholerae* (serogroups O1 and O139) is the causative agent of cholera epidemics, including the outbreak in Haiti (CDC 2010; Chin et al. 2011). Other *Vibrio* species are also pathogenic to humans, including *V. parahaemolyticus*, *V. vulnificus*, and nontoxicogenic *V. cholerae* (nonO1/nonO139), although they are not responsible for widespread epidemics (Chowdhury et al. 2016; Heng et al. 2017; Letchumanan et al. 2014). Rather, they are associated with sporadic cases of gastroenteritis, wound infections, ear infections, and septicemia. *V. parahaemolyticus* is one of the most common bacterial causes of gastroenteritis due to contaminated seafood (Odeyemi 2016) and also causes wound infections on occasions (Ellingsen et al. 2008; Tena et al. 2010).

Whereas death from gastroenteritis due to *V. parahaemolyticus* is rare, the case-fatality rate from primary septicemia or wound infections due to *V. vulnificus* is over 50% (Heymann 2008; Oliver 2005; Torres et al. 2002). For example, following Hurricane Katrina in the United States in 2005, there were 22 new cases of *Vibrio* illness, with five deaths, due to *V. vulnificus*, *V. parahaemolyticus*, or nontoxicogenic *V. cholerae* (CDC 2005). These infections were predominantly present in men over 50 y of age with underlying liver and immune-competency issues.

In all European countries, cholera infection due to *Vibrio cholerae* is a reportable disease, but other *Vibrio* infections are not reportable in all countries. In some countries, screening of patients with diarrheal diseases is only done in travel-related cases. Consequently, accurate estimates of *Vibrio* spp. infections are not available in Europe, although outbreaks of *Vibrio*-associated illnesses have been reported from a number of European countries (Le Roux et al. 2015).

The sea surface temperature (SST) of enclosed bodies of water and estuaries has increased more rapidly as a result of climate change than that of oceans (European Environmental Agency 2012). Elevated SST in brackish water provides ideal environmental growth conditions for *Vibrio* species (Johnson et al. 2012; Julie et al. 2010; Kaspar and Tamplin 1993; Motes et al. 1998; Pfeiffer et al. 2003; Vezzulli et al. 2013; Whitaker et al. 2010). These conditions can be found during the summer months in areas of water with moderate salinity such as the Baltic Sea, Chesapeake Bay in the northeast United States, and the East China Sea around Shanghai. For example, the number of *Vibrio* cases around the Baltic Sea has been found to increase in line with a rise in SST (Baker-Austin et al. 2012); during the summers of 1994, 2003,

Address correspondence to J.C. Semenza, European Centre for Disease Prevention and Control (ECDC), Granits väg 8, 171 65 Solna, Sweden. Telephone: 46 (0)8 58 60 1217. Email: Jan.Semenza@ecdc.europa.eu
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2006, 2010, and 2014 elevated SST across much of the Baltic Sea was associated with reported *Vibrio*-associated illness (Andersson and Ekdahl 2006; Baker-Austin et al. 2016; Dalsgaard et al. 1996; Frank et al. 2006; Lukinmaa et al. 2006; Ruppert et al. 2004). In contrast, open ocean environments do not usually provide suitable growth conditions for these bacteria due to their high salinity, low temperature, and limited nutrient content.

Monitoring is critical, given the projected increase in SST in the future and the potential severity of *Vibrio* infections (Lindgren et al. 2012). More specifically, monitoring the environmental context for such infectious diseases can serve as an early warning system for public health (Nichols et al. 2014; Semenza et al. 2013; Semenza 2015). The European Centre for Disease Prevention and Control (ECDC) developed a quasi-real-time, Web-based platform, the ECDC *Vibrio* Map Viewer, to monitor environmentally suitable marine areas for *Vibrio* growth (ECDC 2016).

This paper presents evidence from marine environments around the world showing that the ECDC *Vibrio* Map Viewer can detect environmental changes that are of public health importance. It relates environmental data from the ECDC *Vibrio* Map Viewer to epidemiological data and, more specifically, assesses the relationship between SST in the Baltic Sea and *Vibrio* infections in Sweden. It also presents the risk of *Vibrio* infections along the Swedish Baltic Sea coast in relation to increasing SST due to climate change under RCP scenarios 4.5 and 8.5.

Methods

ECDC *Vibrio* Map Viewer

The ECDC *Vibrio* Map Viewer (<https://e3geoportal.ecdc.europa.eu/SitePages/Vibrio%20Map%20Viewer.aspx>) displays coastal waters with environmental conditions that are suitable for *Vibrio* spp. growth internationally (Figure 1). It is based on a real-time model that uses daily updated remotely sensed SST and sea surface salinity (SSS) of coastal waters (see below) as inputs to map areas of high suitability for *Vibrio* spp. that are pathogenic to humans (Copernicus Marine Environment Monitoring Service 2016; NOAA 2016). SST and SSS are two key environmental factors that influence the number of infections, based on a model developed by Baker-Austin et al. (2012). For the Baltic Sea, SSS demarcates the regions suitable for *Vibrio* infections (Copernicus Marine Environment Monitoring Service 2016) and SST serves as a risk predictor (NOAA 2016). Salinity in coastal waters is strongly modified by rainfall and, in turn, by river flow; the model uses a threshold of 26 practical salinity units (PSU) for SSS and 18°C for SST. The nominal spatial resolution of the output is 5 km. The daily suitability index ranges from zero to a maximum that is determined by the highest SST value. Thus, the output detects coastal areas with environmental conditions suitable for *Vibrio* species that can cause infections in humans. These fields, which are estimated on a daily basis by the National Oceanic and Atmospheric Administration's (NOAA) Atlantic OceanWatch node at the Atlantic Oceanographic and Meteorological Laboratory (AOML) in Miami, Florida, are integrated within the ECDC *Vibrio* Map Viewer, which is the point of access in the Baltic region.

Environmental Data

In the Baltic Sea, low-salinity areas delineate the areas suitable for the occurrence of *Vibrio* infections, whereas SST serves as a risk predictor (Baker-Austin et al. 2012); however, the influence of SST and SSS on the environmental suitability for *Vibrio* growth can be extrapolated to other regions of the world to obtain global risk estimates. The ECDC *Vibrio* Map Viewer was

designed to delineate retrospective, current, and short-term forecasts of environmental suitability at a global scale, which requires obtaining reliable SST and SSS, especially in coastal regions where human exposure is more likely to occur (Figure 1). The global model data inputs are SST fields from remote sensing and models, as well as SSS from models, *in situ* data, and climatological data. The estimates for SST were obtained from a number of sources:

- USDOC/NOAA/NESDIS (U.S. Department of Commerce/NOAA/National Environmental Satellite Data and Information Service) COASTWATCH NOAA19/METOP-A/GOES-E/W MSG/MTSAT SST Blended Analysis
- NOAA/NCEP (National Centers for Environmental Prediction) Global Real-Time Ocean Forecast System
- Navy Coastal Ocean Model (NCOM) for the Gulf of Mexico, Caribbean, and U.S. East Coast
- Operational Mercator Global Ocean Analysis and Forecast System
- Iberian Biscay Irish (IBI) Ocean Analysis and Forecasting system
- Forecasting Ocean Assimilation Model 7 km Atlantic Margin model (FOAM AMM7)
- Baltic Sea Physical Analysis and Forecasting Product
- Mediterranean Sea Physics Analysis and Forecast
- Black Sea Physics Analysis and Forecast

SSS were obtained from the Copernicus Marine Environment Monitoring Service (2016). For retrospective studies, NOAA's Optimum Interpolation (OI) SST V2 data set provided satellite and model-interpolated daily analysis of SST in a consistent methodology back to September 1981. For the Swedish coastal counties, mean SST were spatially aggregated per county per week for the years of analysis (2006–2014) to generate time-series data sets for each coastal county.

Climate change projections of SST were derived from a Coupled Model Intercomparison Project Phase 5 (CMIP5) model ensemble (r1i1p1) for the Swedish coastline aggregated by county. Time series per month for each county from 2005 through 2100 were derived. Model output was obtained for emission scenarios RCP 4.5 and RCP 8.5, representing a possible range of radiative forcing values in the year 2100 relative to preindustrial values (+4.5, and +8.5 W/m², respectively).

Case Data

Infections caused by *Vibrio cholerae* (other than serotypes O1 or O139 and *Vibrio cholerae* serotype O1 or O139, which are non-toxigenic) are notifiable according to the Swedish Communicable Diseases Act (Swedish Code of Statutes 2004) and include *V. parahaemolyticus*, *V. vulnificus*, and *V. alginolyticus*. Cases are reported to the mandatory notification system at the county medical office and at the Swedish Public Health Agency. We obtained a listing of all *Vibrio* infections from 2006 through 2014 with clinical and laboratory confirmation from the Swedish Public Health Agency (Folkhelsomyndigheten 2016). The listing included information on county, statistical date and onset of disease, type of infection, *Vibrio* species, serotype, transmission pathway, sex, and age group of each case. For reasons including consistency in reporting and data completeness, we used data for the period 2006 through 2014 for our analysis. A total of 117 cases were reported for the period from June 2006 through October 2014, of which 111 occurred in coastal counties with a possible link to SST. Thus, being in close proximity to the Baltic provides the opportunity for exposure to coastal water both for case and control times. However, 30 of these cases had no precise place of infection and 25 cases had no date of onset of disease, and these cases were not included in the analysis.

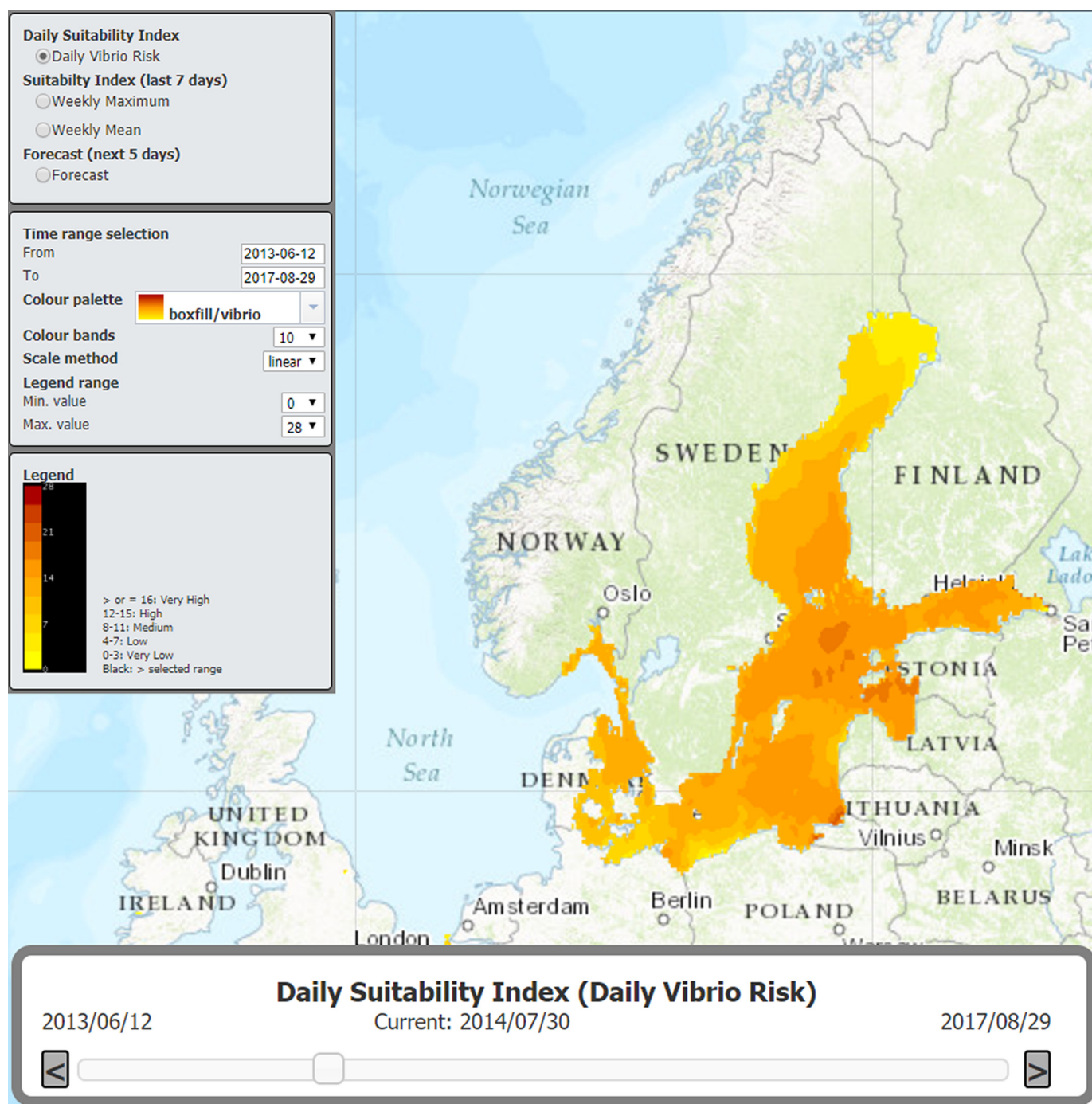


Figure 1. ECDC *Vibrio* Map Viewer: environmental suitability for *Vibrio* spp., July 2014, Baltic Sea. Source: Reproduced from <https://e3geoportal.ecdc.europa.eu/SitePages/Vibrio%20Map%20Viewer.aspx>, © European Centre for Disease Prevention and Control.

Statistical Analyses

The variables of the 56 *Vibrio* cases for 2006–2014 were subjected to descriptive statistics and frequency analysis. Because changes in SST occur intermittently, have a short induction time and a transient effect (Vibriosis), a case-crossover study design was chosen to assess the association between SST and *Vibrio* infections. The SST exposure status (mean SST, spatially aggregated per county and per week) of the *Vibrio* infection at the time of the Vibriosis onset was compared with the distribution of the SST exposure status for that same Vibriosis case in earlier/later periods. This approach assumes that neither exposure nor confounders change over the study period in a systematic way. Thus, a time-stratified

approach at the individual level was used for control days to contrast with the events. An advantage of using such a time-stratified case-crossover design is the automatic adjustment for individual non-time varying factors; these can risk introducing confounding bias in epidemiological studies if not adjusted for. Further, the time-stratified approach used control events before and after the event date for each individual *Vibrio* infection in the same area. We used 2, 4, and 6 wk as the time window between event data and the control days, both before and after the event. This adjusts for unknown temporal confounders and controls for seasonal influences not related to the seasonality of SST as the primary exposure variable.

The weekdays of the dates of the weekly county means of the SSTs were restricted to Mondays, but the date of infection was for any date. Thus, in order to match the date of infection with its corresponding SST, Tuesday to Thursday were referred to the preceding Monday, whereas Friday to Sunday were referred to the following Monday. For analysis, a data set with the event itself and control events 2, 4, and 6 wk before and after the event was created. A time series with SST county means from 1 to 8 wk before the event and the controls was added.

We used a conditional logistic regression model to ascertain a relationship between SST and *Vibrio* infection and to derive an exposure–response curve for the relationship between the odds ratio of *Vibrio* infection and SST. We refer to the odds ratio analogously to relative risk in this study due to the low probability of disease events. We studied the relationship between *Vibrio* infections and SST using natural cubic splines (4 degrees of freedom) and for different lead times of exposure up to 4 wk before disease occurrence. We identified a piecewise linear model with a knot of SST at 16°C for the final model.

We used the computed case-crossover exposure–response relationship to project how the seasonal window of transmission would change in each of the counties. We used projections of SST data from a global circulation model from CMIP5 for each month in the time period from 2006 through 2099 for each county. Months with elevated risk were categorized as potential transmission months and aggregated as average per decades. The annual maximum elevated risk month was averaged to a change of transmission intensity per decade. Relative risk estimates are presented using the year 2016 as the baseline and describe changes due to SST from there onward.

We used also CMIP5 sea surface temperature projections for the RCP projections to illustrate differences in the projected SST between RCP 8.5 and RCP 4.5 for August 2050. We computed the surface area [in kilometers squared (km²)] of the Baltic Sea that is environmentally suitable for *Vibrio* growth for RCP 4.5 and RCP 8.5, from 2010 through 2060, by month.

Results

In July 2014, SST in the Baltic Sea reached record highs and the ECDC *Vibrio* Map Viewer detected environmentally suitable areas for *Vibrio* spp. (Figure 1). High *Vibrio* suitability was detected in the northern and the southern parts of the Baltic Sea in mid-July, and this extended to the entire Baltic Sea by the end of the month.

The annual frequency of total *Vibrio* cases notified in Sweden from 2006 through 2014 is presented in Figure 2. A peak in cases was observed in 2006 and in 2014, compared with other years. *Vibrio* infections other than CTX (cholera toxin)-producing *V. cholerae* (O1 or O139) reported in Sweden, included in the case-crossover analysis, are listed in Table 1. The majority of infections were detected in the ear (50%), but wound infections (28%) and septicemia (20%) combined constituted almost half of all infections. Only a small fraction of the samples found pathogens in stool, saliva, or urine (2%). A time series analysis of the site of infection did not reveal a time trend in *Vibrio* infections, with the exception of wound infections that indicated an increase. Almost one-third (30%) of the cases were ≥60 y of age, 25% were 10–19 y of age, 25% were 20–59 y of age, and 20% were ≤9 y of age.

The SSTs along the Swedish coast were interpolated for the study period (2006–2014). An exposure–response relationship was estimated with a case-crossover study; additional non-disease (no *Vibrio* infections) time periods with the corresponding SST were selected as matched control periods for each *Vibrio* infection. The estimated exposure–response relationship for

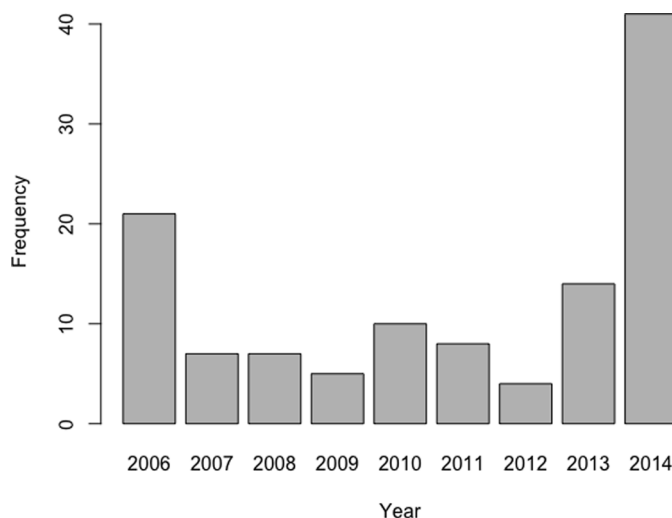


Figure 2. Annual frequency of total *Vibrio* infections notified in Sweden, 2006–2014.

Vibrio infections in response to SST is shown in Figure 3. At the threshold of 16°C SST, with a lag of 2 wk, the relative risk (RR) was 1.14 [95% confidence interval (CI): 1.02, 1.27]. The relationship between *Vibrio* infections and SST was statistically significant ($p=0.024$), and the estimated risk increased successively beyond a threshold of 16°C SST. However, that relationship did not hold at lower SST. Case data were available with a statistical date and a date of onset of disease. The date of onset of disease correlated to the SST of the same week and with lags up to 2 wk, whereas the statistical date, which is the first date when the case was reported to the national notification system for the cases correlated best with lags between 2 and 4 wk.

Climate change projections for SST under the RCP 4.5 and RCP 8.5 scenarios for the 21st century were used to estimate the relative risk of *Vibrio* infections in the future. A global comparison of the SST between RCP 4.5 and RCP 8.5 for August 2050 is shown in Figure 4A, which illustrates a general warming overall, but also regional cooling in certain locations, such as the Baltic Sea (Figure 4B). The monthly projection of SST suitability for *Vibrio* in the Baltic Sea up to 2060 is provided in Figure 5. A marked upward trend is observed for SST during July, August, and September but even more so during the months immediately prior to and after the summer (June and October).

The area suitable for *Vibrio* growth is projected to expand over the coming decades, particularly during June and September (Figure 6), doubling between 2015 and 2050. In July 2015, the area of risk was 140,000 km²; for scenario RCP 4.5, the area of risk would reach 309,966 km² in July 2050 and for RCP 8.5, 317,793 km² in July 2050. Figure 7 shows Baltic Sea areas suitable for *Vibrio* growth during the months of June, July, August, and September 2016 and for RCP 4.5 and RCP 8.5 in 2050. The RCP 8.5 scenario for 2050 gives a lower maximum SST than RCP 4.5 (Figure 7); although at global level, the rise in temperature is higher with RCP 8.5 (Figure 4), and at a regional level, RCP 4.5 gives higher temperatures for this particular year. The difference is significant and at some point the differences between the two models can reach up to 2°C. This discrepancy is also visible in the isotherms for the difference between 2015 and projections for 2050 under RCP 4.5 and RCP 8.5 by month (see Figure S1).

The change in relative risk (%) for *Vibrio* infections in comparison with 2015 is illustrated in Figures 8 and 9 for the coastline of Sweden for RCP 4.5 and RCP 8.5. A marked increase in the relative risk was predicted beyond the year 2039 for both

Table 1. *Vibrio* infections other than *Vibrio cholerae*, included in the case-crossover analysis, reported in Sweden by site of infection, species, age, sex, region, 2006 through 2014.

Demographic data	Cases (n)
Male	82
Female	35
Age	
Mean (y)	40.9
SD (y)	29
Range (y)	2–94
Route of infection	
Blood	20
Ear	59
Feces	3
Mouth	1
Urine	1
Wound	33
<i>Vibrio</i> spp.	
<i>V. alginolyticus</i>	13
<i>V. parahaemolyticus</i>	14
<i>V. vulnificus</i>	3
<i>V. cholerae</i> (not CTX producing)	48
<i>Vibrio</i> species (not agglutinating <i>V. cholerae</i>)	39
Counties	
Blekinge	6
Gotland	1
Gävleborg	6
Halland	9
Jämtland	1
Jönköping	4
Kalmar	3
Kronoberg	5
Skåne	27
Stockholm	21
Uppsala	4
Värmland	3
Västerbotten	3
Västernorrland	3
Västra Götaland	15
Örebro	3
Östergötland	3

scenarios and, toward the end of the 21st century, the change in relative risk was particularly pronounced for the RCP 8.5 scenario.

Potential transmission months, defined by an elevated risk for *Vibrio* infections based on the SST, were aggregated as averages per decades (see Figures S2 and S3). The transmission season is and will be longer in the southern part of Sweden compared with the northern part. Under climate change scenarios RCP 4.5 and RCP 8.5, the number of months with risk of *Vibrio* transmission increases; the seasonal transmission window expands, with markedly higher increases of months with transmission for the high emission scenario RCP 8.5. However, the impact of climate change becomes more prominent in the northern part after the year 2039 when the transmission season reaches the current levels of southern Sweden.

Discussion

In July 2014, the ECDC *Vibrio* Map Viewer detected highly suitable conditions for *Vibrio* infections in the Baltic Sea (Figure 1) and the mandatory notification system at the Swedish Public Health Agency reported a historic peak of Vibriosis cases for 2014 (Figure 2). We demonstrate with a case-crossover study that the reported *Vibrio* infections are related to these favorable environmental conditions; we found a pronounced exposure–response relationship between SST and *Vibrio* infections (Figure 3). Climate change projections indicate that the risk for *Vibrio* infections will increase in the 21st century: The

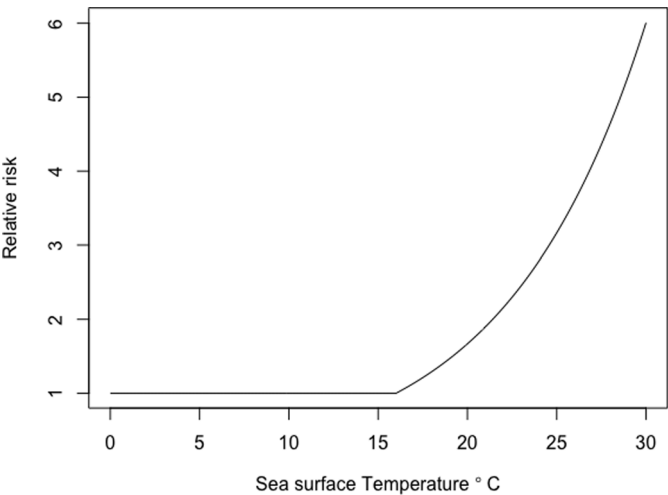


Figure 3. Exposure–response relationship of *Vibrio* infections in response to sea surface temperature (SST), Sweden 2006–2014. Note: Because *Vibrio* infections in the Baltic are relatively rare, the relative risk is used here analogously to the odds ratio.

transmission season will be expanded and the number of months with risk of *Vibrio* transmission will increase, particularly in the northern latitudes of the Baltic Sea. SST in the Baltic Sea is projected to increase by 4–5°C over the next decades due to climate change.

The 5-d forecasting function available on the ECDC *Vibrio* Map Viewer can serve as an early warning system for *Vibrio* infections in the Baltic Sea (Figure 1). Currently, ECDC monitors the environmental suitability for *Vibrio* infections in the Baltic Sea with the ECDC *Vibrio* Map Viewer on a weekly basis and, during the transmission season, publishes the findings in its Communicable Disease Threat Reports (CDTR). This enables public health authorities to take action, such as issuing alerts to the public or information to immunocompromised individuals or even beach closures. The European Environmental Agency provides information on bathing water quality, based on actual measurements of bacterial contamination (intestinal enterococci and *Escherichia coli*) of recreational water sites (European Environmental Agency 2016), whereas the alerts from the ECDC *Vibrio* Map Viewer are based on estimates of environmental suitability for *Vibrio* infections, not actual risk because no exposure data are available for such an assessment.

Globalization, through international travel and trade, is an important driver of emerging infectious diseases (Semenza et al. 2016), including virulent *Vibrio* strains, and can synergistically interact with other drivers such as climate change (Semenza and Menne 2009). A new serotype of *V. parahaemolyticus* (O3:K6) has emerged in Asia and has spread rapidly to South America (González-Escalona et al. 2005; Martínez-Urtaza et al. 2008). The pandemic expansion of this strain is associated with large-scale food-borne disease outbreaks (Yeung et al. 2002). Other virulent *V. parahaemolyticus* strains (O4:K12 and O4:KUT) have recently spread from the Pacific Northwest to the Atlantic coasts of the United States and Spain (Martínez-Urtaza et al. 2013; McLaughlin et al. 2005).

The ECDC *Vibrio* Map Viewer can also be used to detect suitability for *Vibrio* growth in other settings. For example, for gastrointestinal infections in estuarine environments, to assess the environmental suitability for *Vibrio* growth in oyster and other shellfish farms that might warrant a temporary harvesting ban. In the summer of 2012, outbreaks of *V. parahaemolyticus* infection caused by Pacific Northwest strains occurred on the

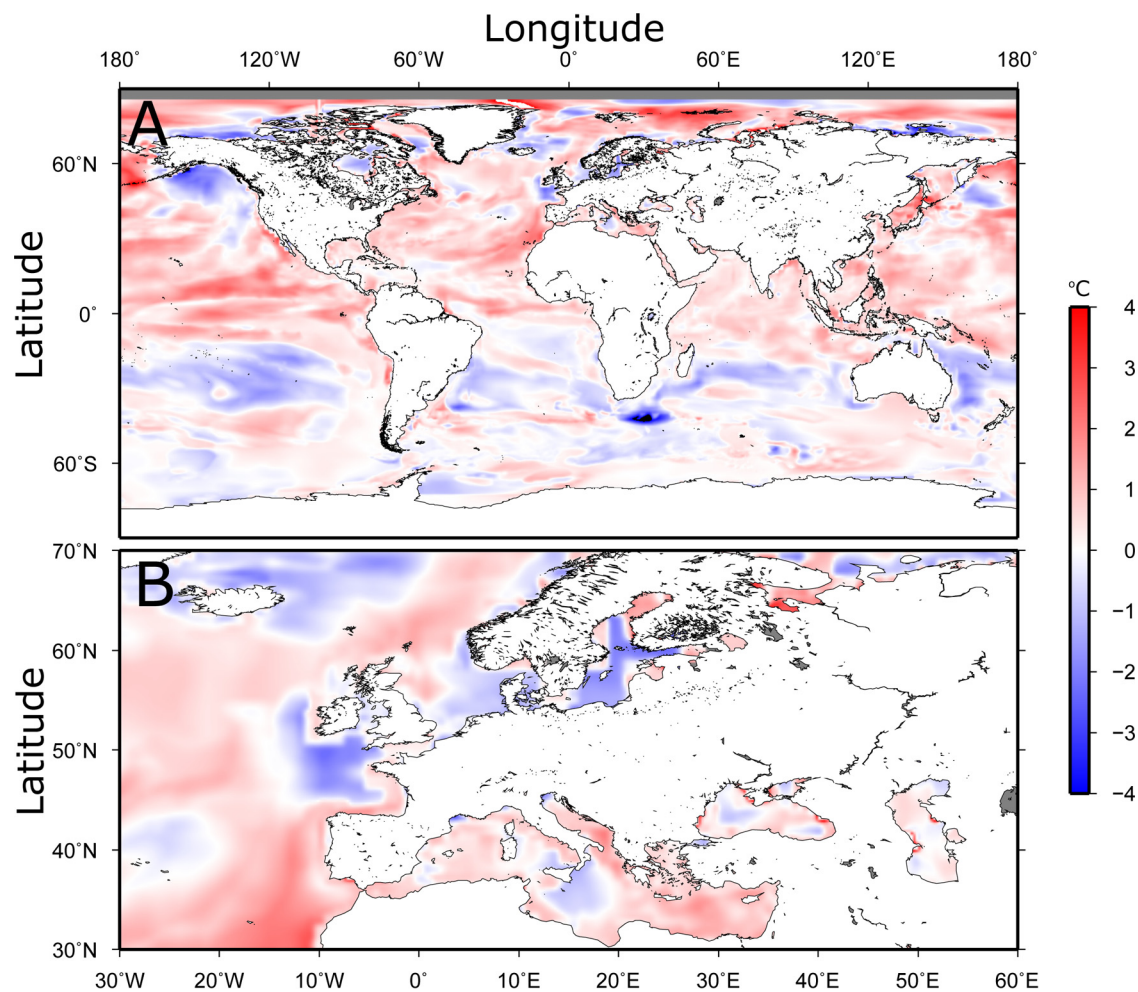


Figure 4. Difference of sea surface temperature (SST) between RCP 4.5 and 8.5 for August 2050: (A) global and (B) regional. Note: Climate model for RCP projections: CMIP5 SST projection that uses various models (86 total). The figures were created using a data set from a contribution to GEOSS Data-Core (GEOSS Data Collection of Open Resources for Everyone), as a result of the GEOWOW (GEOSS interoperability for Weather, Ocean and Water) project. Data are licensed under Creative Commons CC-BY-4.0 (as defined in <http://www.opendefinition.org/licenses/cc-by>), which allows redistribution and re-use. Data sources: [Combal 2014a, 2014b, 2014c](#). Difference RCP 8.5–4.5: Difference in the projected SST between RCP 8.5 and RCP 4.5 for August 2050. RCP 8.5 projections are in general warmer than RCP 4.5 ones. However, the distribution and intensity of the differences are inhomogeneous and highly variable. The values are predominantly positive but negative values are shown in the Baltic Sea during this period.

Atlantic coast of the United States ([Martinez-Urtaza et al. 2013](#)); this was the first multistate outbreak of *V. parahaemolyticus* illnesses reported in the United States for almost a decade. A total of 12 confirmed and 16 probable outbreak-associated cases were reported between 24 April and 3 August ([Newton et al. 2014](#)). Illness onset dates ranged from 27 May to 20 July 2012. The median age of patients was 49 y and 46% were female. Two patients were hospitalized; none died. The outbreak was linked to consumption of shellfish harvested from Oyster Bay Harbor in New York State between April and August 2012. The Rhode Island Department of Health advised food establishments to check the tags on any shellfish that they were selling to consumers or using in food preparation and to avoid selling or using shellfish harvested from the Oyster Bay area. Harvesting of shellfish from the area was temporarily prohibited on 13 July. The suitability for *Vibrio* growth in this area was detected by the ECDC *Vibrio* Map Viewer (see Figure S4).

During the summer of 2015, a total of 81 cases were reported in Canada between 26 May and 26 August. Cases of *V. parahaemolyticus* were identified in British Columbia (60), Alberta (19), Saskatchewan (1), and Ontario (1), and one case needed to be hospitalized. No deaths were reported. The majority of cases were linked

to consumption of raw shellfish, primarily oysters. Oysters harvested from British Columbia coastal waters for raw consumption on or before 18 August were recalled from the market by the Canadian Food Inspection Agency. The suitability for *Vibrio* growth in these areas was also detected by the ECDC *Vibrio* Map Viewer (see Figure S5) and the trend for SST (see Figure S6).

Global sea level rise due to climate change is also projected to result in the flooding of low-lying coastal areas, resulting in expansion of estuarine and brackish environments ([Semenza et al. 2012](#)). Both phenomena may contribute to the proliferation and geographic expansion of bacterial pathogens of marine and estuarine environments ([Ebi et al. 2017](#); [Jacobs et al. 2015](#); [Levy 2015](#)). The ECDC *Vibrio* Map Viewer can play an important public health role in view of the ubiquitous presence of *Vibrio* spp. in brackish coastal water. Although the burden of disease from these pathogens is relatively low, the severity of the high case fatality for susceptible individuals from primary septicemia is nevertheless a concern.

Limitations

The ECDC *Vibrio* Map Viewer displays environmental suitability for *Vibrio* infections based on SST and SSS ([Copernicus Marine](#)

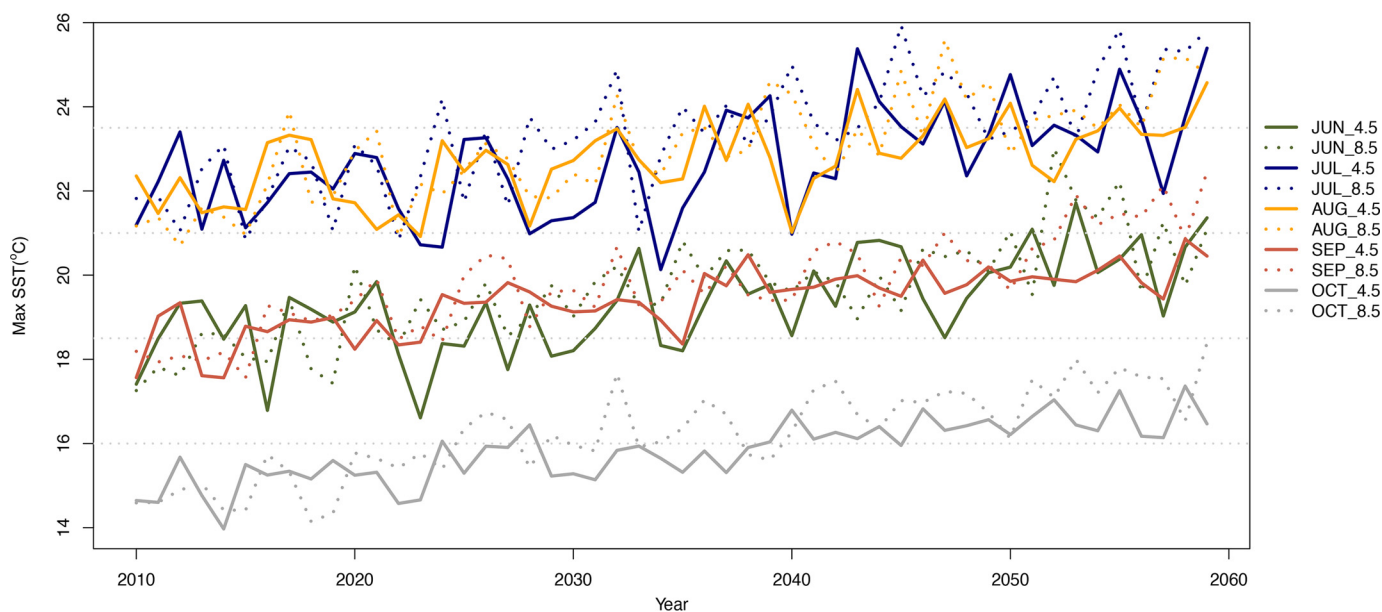


Figure 5. Suitability for *Vibrio* based on SST in the Baltic Sea for RCP 4.5 and RCP 8.5, from 2010 through 2058, by month. Note: The figures were created using a data set from a contribution to GEOSS Data-Core (GEOSS Data Collection of Open Resources for Everyone), as a result of the GEOWOW (GEOSS interoperability for Weather, Ocean and Water) project. Data are licensed under Creative Common CC-BY-4.0 (as defined in <http://www.opendefinition.org/licenses/cc-by>), which allows redistribution and re-use. Data sources: Combal 2014a, 2014b, 2014c.

Environment Monitoring Service 2016; NOAA 2016). However, *Vibrio* ecology and growth also depend on a number of other variables including marine nutrient concentrations, river discharge, and algae blooms (Boer et al. 2013; Johnson et al. 2012; Julie et al. 2010). For example, long-distance atmospheric deposition and aerosols such as Saharan dust nutrients can promote *Vibrio* bloom formation in marine surface waters (Ansmann et al. 2003; Westrich et al. 2016). Moreover, individual *Vibrio* species display different responses in relation to SST and SSS (Boer et al.

2013; Johnson et al. 2012; Julie et al. 2010). Thus, the environmental suitability shown by the ECDC *Vibrio* Map Viewer represents an approximation of the actual suitability and local variation might apply. In addition, many *Vibrio* infections are influenced by other factors, such as immunity, travel, and gastrointestinal disease, in addition to coastal water exposure. Currently, the Swedish Public Health Agency recommends that people avoid swimming if they have a significant or open wound and the SST is 20°C or higher.

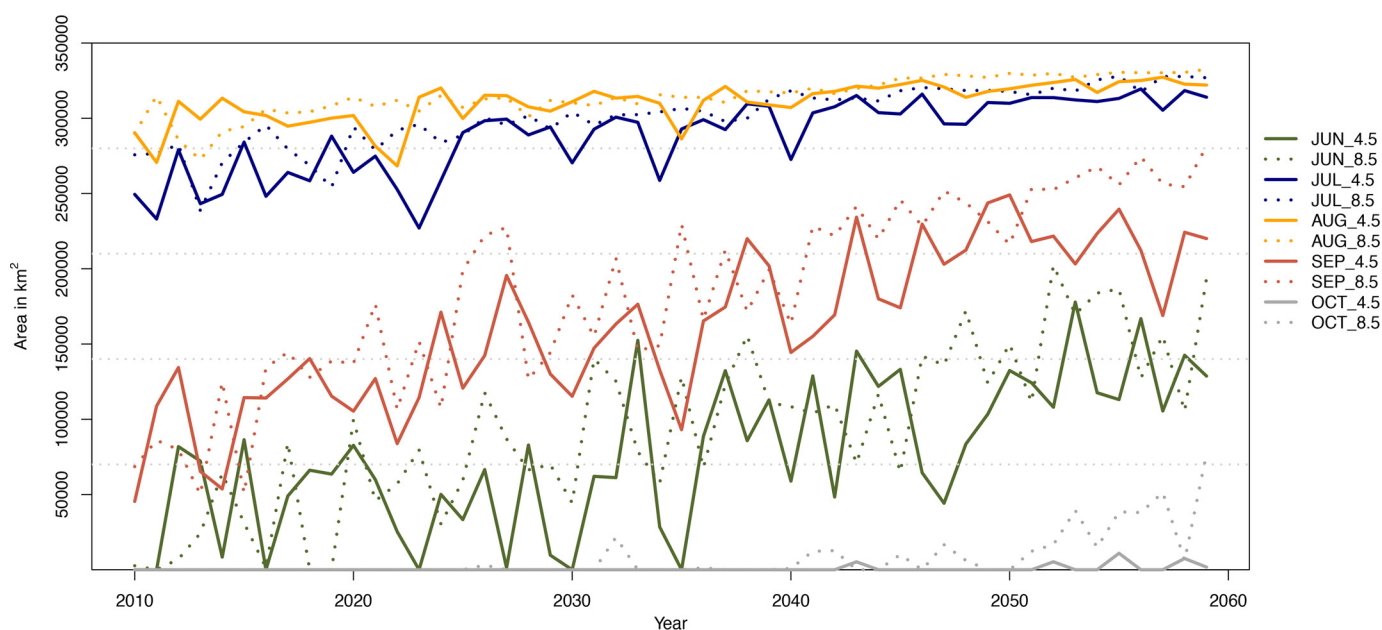


Figure 6. Surface area (km²) of the Baltic Sea that is environmentally suitable for *Vibrio* growth for RCP 4.5 and RCP 8.5, from 2010 through 2060, by month. Note: The figures were created using a data set from a contribution to GEOSS Data-Core (GEOSS Data Collection of Open Resources for Everyone), as a result of the GEOWOW (GEOSS interoperability for Weather, Ocean and Water) project. Data are licensed under Creative Common CC-BY-4.0 (as defined in <http://www.opendefinition.org/licenses/cc-by>), which allows redistribution and re-use. Data sources: Combal 2014a, 2014b, 2014c.

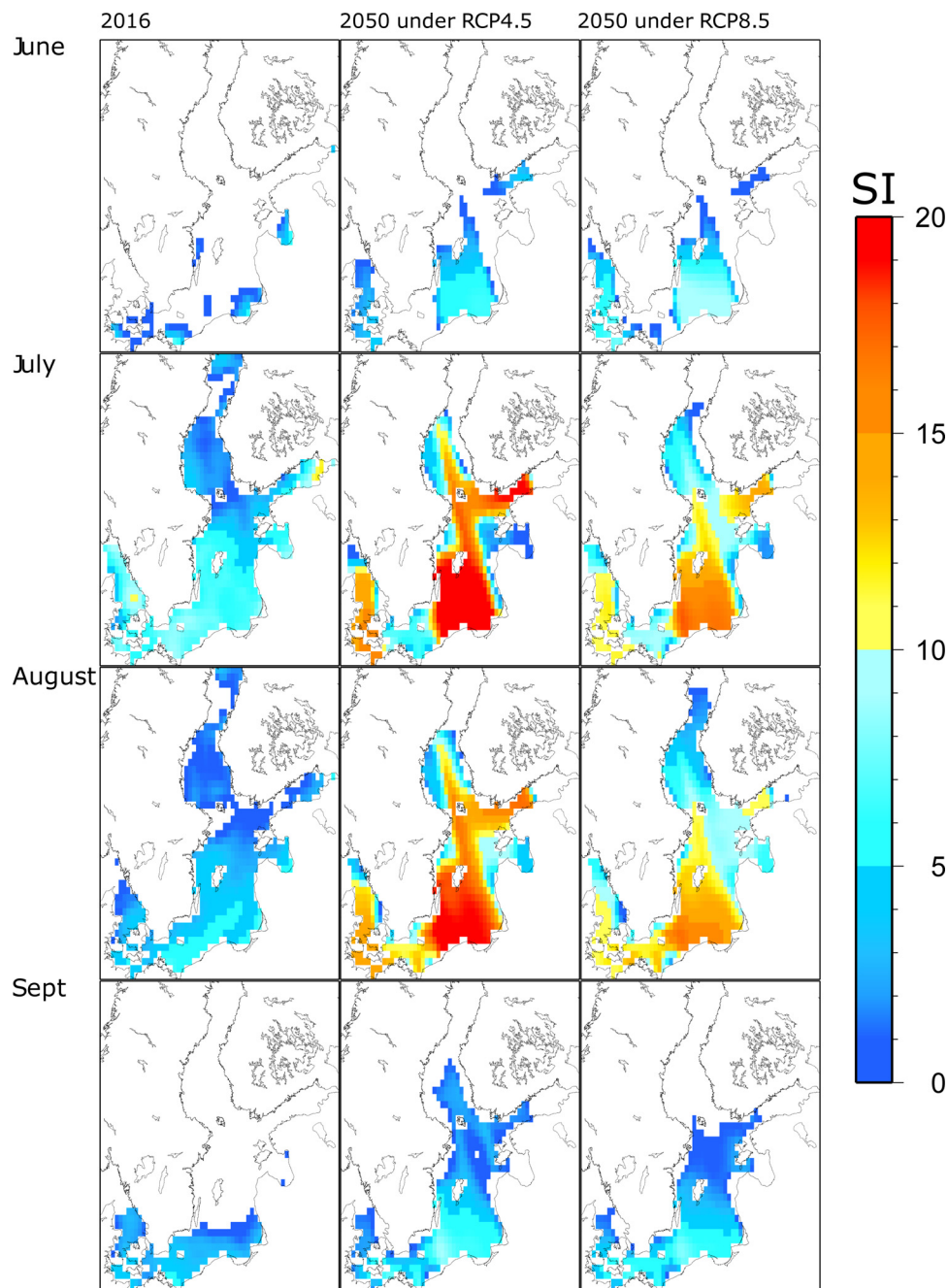


Figure 7. Environmental suitability for *Vibrio* based on maximum SST for 2016, for 2050 with RCP4.5, and for 2050 with RCP8.5, for June, July, August, and September. Note: Environmental suitability fields in the Baltic Sea during June, July, August, and September: low-salinity areas delineate the region suitable for the occurrence of infections, whereas SST serves as a risk predictor. The left column shows the fields estimated for the year 2016. The center and right columns show the projected suitability index (SI) for the year 2050, under RCP 4.5 and RCP 8.5, respectively. In both cases, there is an important increment in the mean values of the SI ($SI > 10$) when compared with the year 2016. The figures were created using a data set from a contribution to GEOSS Data-Core (GEOSS Data Collection of Open Resources for Everyone), as a result of the GEOWOW (GEOSS interoperability for Weather, Ocean and Water) project. Data are licensed under Creative Commons CC-BY-4.0 (as defined in <http://www.opendefinition.org/licenses/cc-by>), which allows redistribution and re-use. Data sources: Combal 2014a, 2014b, 2014c.

Our analysis was based on Swedish data because *Vibrio* infections became reportable in Sweden in 2004. In many other Baltic countries, *Vibrio* infections are not reportable and therefore, little information is available to assess the risk in those countries. Regrettably, there was not a training data set and a testing data set to validate the exposure–response relationship of *Vibrio* infections in response to SST. However, our findings are consistent with the documented number and distribution of

Vibrio infections clustered around the Baltic Sea area associated with the temporal and spatial peaks in SST (Baker-Austin et al. 2012).

Conclusion

Mortality and morbidity due to *Vibrio* infections continue to occur in the Baltic Sea area. Moreover, we show that the environmental suitability of *Vibrio* growth in the Baltic Sea will expand in a

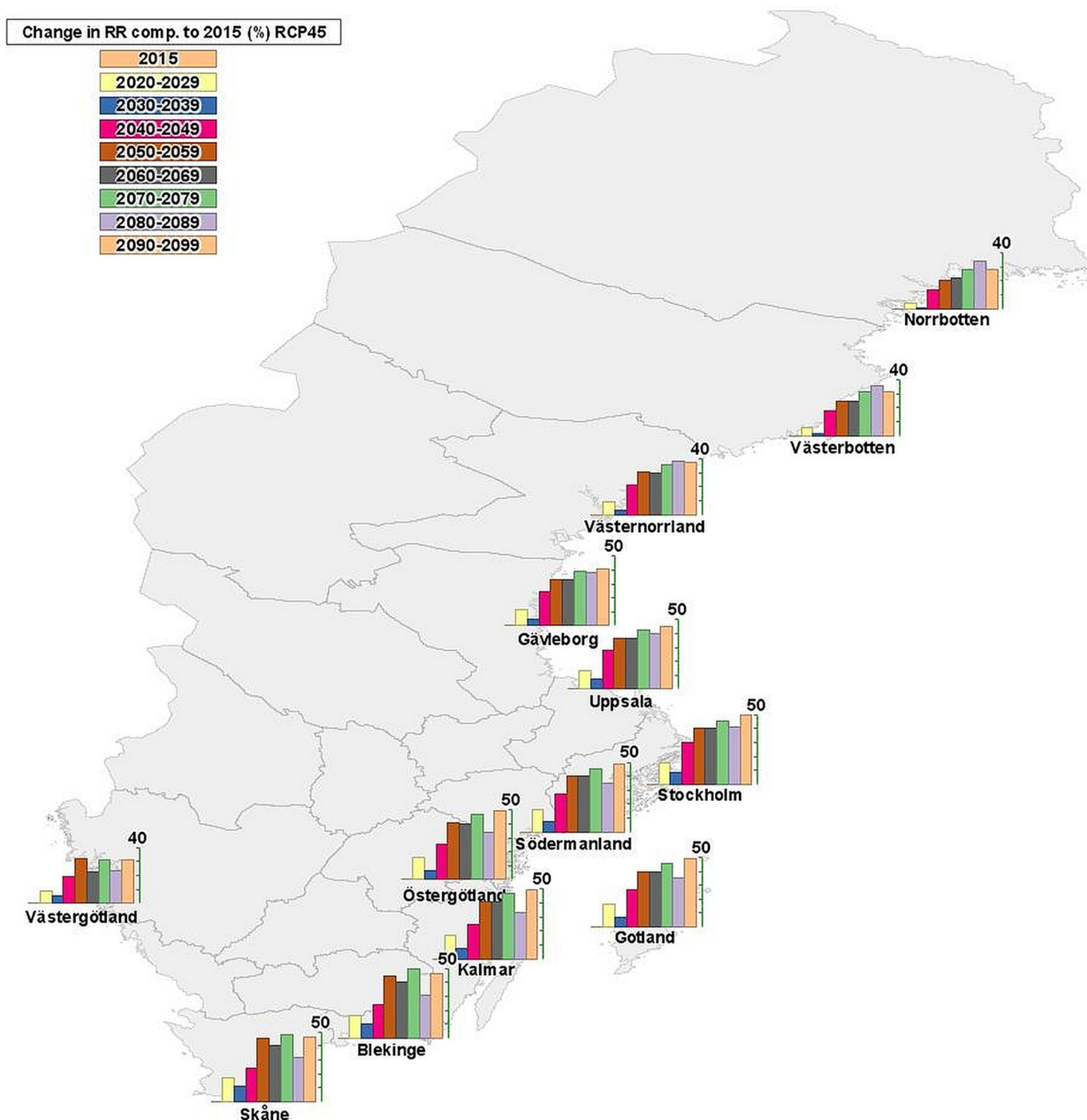


Figure 8. Change in relative risk (%) of *Vibrio* infections associated with climate change scenario RCP 4.5, 21st century.

warming climate. However, in Europe, there is almost a complete lack of information regarding the persistence/abundance of *Vibrio* in the environment and the number of human cases. Reporting of *Vibrio* infections is not mandatory in the European Union, and many laboratories test only for *Vibrio* infections in patients with diarrhea when they are returning from a foreign holiday (to rule out *Vibrio cholerae*). The strength of this study lies in the fact that most of the infections were nongastrointestinal and therefore not subject to this selection bias. Thus, in the absence of mandatory notification data on *Vibrio* infections in Europe, the ECDC *Vibrio* Map Viewer can forecast the environmental suitability of coastal

waters for *Vibrio* spp. using remotely sensed SST and SSS. These forecasts and potential alerts are currently disseminated by ECDC to public health decision makers, along with different response options for their consideration, through the CDTR: Public access to a beach should be temporarily denied for public safety purposes, warnings should be issued when the environmental suitability of *Vibrio* infections is imminent, or alerts should be issued to notify health care providers and at-risk individuals such as the immunocompromised. Through this cascade of steps—risk assessment, monitoring of environmental suitability and alert detection, dissemination and communication, and response—the ECDC *Vibrio* Map

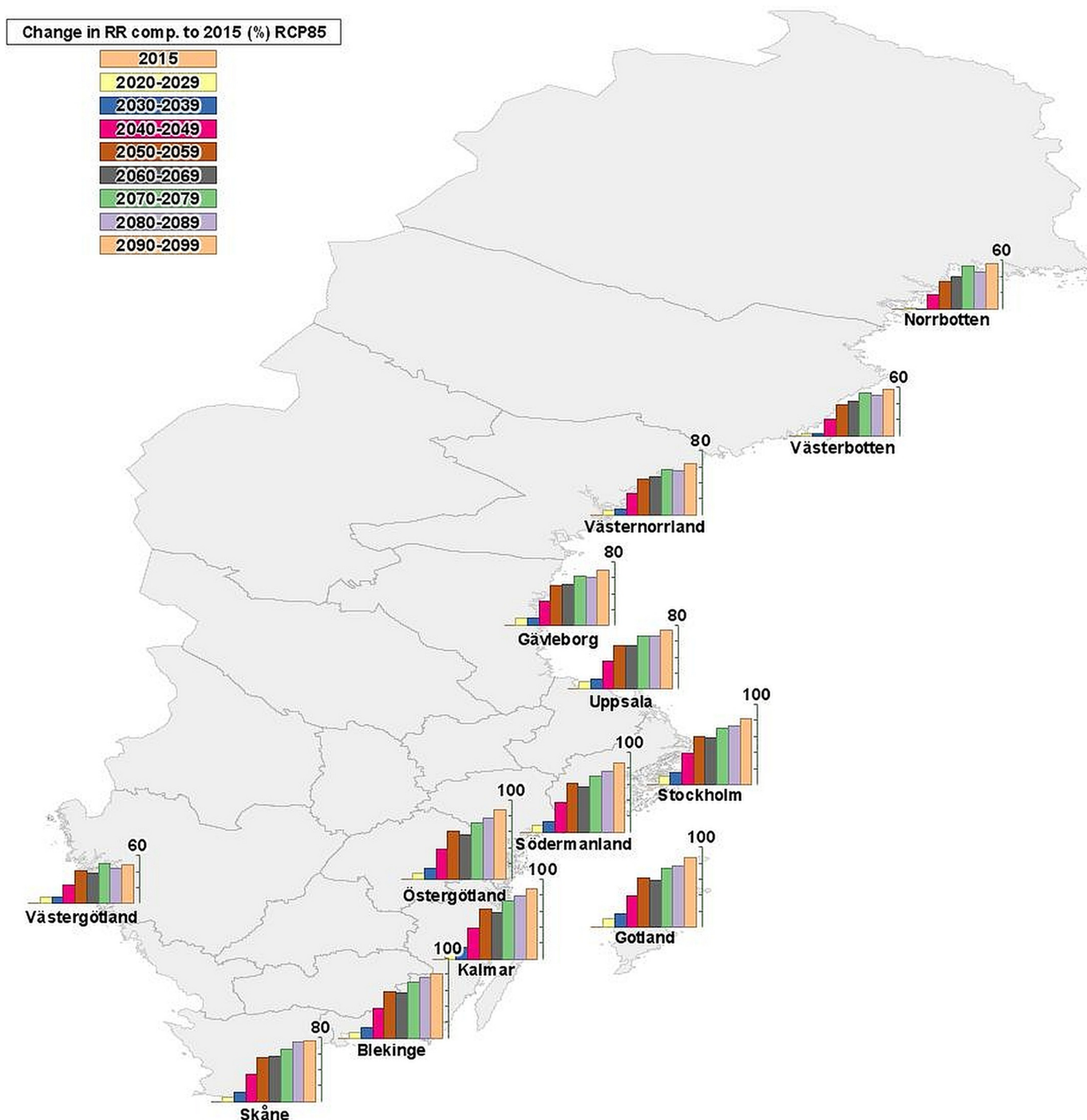


Figure 9. Change in relative risk (%) of *Vibrio* infections associated with climate change scenario RCP 8.5, 21st century.

Viewer constitutes an important link in an early warning system for *Vibrio* infections.

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References

- Andersson Y, Ekdahl K. 2006. Wound infections due to *Vibrio cholerae* in Sweden after swimming in the Baltic Sea, summer 2006. *Euro Surveill* 11(8): E060803.060802, PMID: [16966771](https://pubmed.ncbi.nlm.nih.gov/16966771/).
- Ansmann A, Bösenberg J, Chaikovskiy A, Comerón A, Eckhardt S, Eixmann R. 2003. Long-range transport of Saharan dust to northern Europe: the 11–16 October 2001 outbreak observed with EARLINET. *J Geophys Res Atmos* 108(D24), <https://doi.org/10.1029/2003JD003757>.
- Baker-Austin C, Trinanès JA, Salmenlinna S, Löfdahl M, Siitonen A, Taylor NG, et al. 2016. Heat wave-associated vibriosis, Sweden and Finland, 2014. *Emerg*

- Infect Dis 22(7):1216–1220, PMID: 27314874, <https://doi.org/10.3201/eid2207.151196>.
- Baker-Austin C, Trinanet J, Taylor N, Hartnell R, Siitonen A, Martinez-Urtaza J. 2012. Emerging *Vibrio* risk at high latitudes in response to ocean warming [Letter]. *Nat Clim Chang* 3(1):73–77, <https://doi.org/10.1038/nclimate1628>.
- Boer SI, Heinemeyer EA, Luden K, Erler R, Gerdt G, Janssen F, et al. 2013. Temporal and spatial distribution patterns of potentially pathogenic *Vibrio* spp. at recreational beaches of the German North Sea. *Microb Ecol* 65(4):1052–1067, PMID: 23563708, <https://doi.org/10.1007/s00248-013-0221-4>.
- CDC (Centers for Disease Control and Prevention). 2005. *Vibrio* illnesses after Hurricane Katrina—multiple states, August–September 2005. *MMWR Morb Mortal Wkly Rep* 54:928–931, PMID: 16177685, <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5437a5.htm>.
- CDC. 2010. Cholera outbreak—Haiti, October 2010. *MMWR Morb Mortal Wkly Rep* 59:1411, PMID: 21048563.
- Chin CS, Sorenson J, Harris JB, Robins WP, Charles RC, Jean-Charles RR, et al. 2011. The origin of the Haitian cholera outbreak strain. *N Engl J Med* 364(1):33–42, PMID: 21142692, <https://doi.org/10.1056/NEJMoa1012928>.
- Chowdhury G, Joshi S, Bhattacharya S, Sekar U, Birajdar B, Bhattacharyya A, et al. 2016. Extraintestinal infections caused by non-toxicogenic *Vibrio cholerae* non-O1/non-O139. *Front Microbiol* 7:144, PMID: 26904017, <https://doi.org/10.3389/fmicb.2016.00144>.
- Combal B. 2014a. Ensemble mean of CMIP5 TOS, for the period 1971 to 2000 [data set]. Zenodo. <https://doi.org/10.5281/zenodo.12843> [accessed 17 April 2017].
- Combal B. 2014b. Monthly climatology of CMIP5 models historical run, for 1971–2000 [data set]. Zenodo. <https://doi.org/10.5281/zenodo.12943> [accessed 17 April 2017].
- Combal B. 2014c. Time projections of sea surface temperature, for RCP 4.5 and RCP 8.5, for decade 2020, 2030, 2040 and 2040 [data set]. Zenodo. <https://doi.org/10.5281/zenodo.12781> [accessed 17 April 2017].
- Copernicus Marine Environment Monitoring Service. 2016. Copernicus. <http://marine.copernicus.eu/web/69-interactive-catalogue.php> [accessed 17 April 2016].
- Dalsgaard A, Frimodt-Møller N, Bruun B, Høi L, Larsen JL. 1996. Clinical manifestations and molecular epidemiology of *Vibrio vulnificus* infections in Denmark. *Eur J Clin Microbiol Infect Dis* 15(3):227–232, PMID: 8740858, <https://doi.org/10.1007/BF01591359>.
- Ebi KL, Ogden NH, Semenza JC, Woodward A. 2017. Detecting and attributing health burdens to climate change. *Environ Health Perspect* 125(8):085004, PMID: 28796635, <https://doi.org/10.1289/EHP1509>.
- ECDC (European Centre for Disease Prevention and Control). 2016. *Vibrio* Map Viewer. <https://ecdc.europa.eu/SitePages/Vibrio%20Map%20Viewer.aspx> [accessed 17 April 2017].
- Ellingsen AB, Jørgensen H, Wagley S, Monshaugen M, Rørvik LM. 2008. Genetic diversity among Norwegian *Vibrio parahaemolyticus*. *J Appl Microbiol* 105(6):2195–2202, PMID: 19120665, <https://doi.org/10.1111/j.1365-2672.2008.03964.x>.
- European Environmental Agency. 2012. *Climate Change, Impacts and Vulnerability in Europe 2012*. Copenhagen, Denmark: European Environmental Agency.
- European Environmental Agency. 2016. State of Bathing Waters. <http://www.eea.europa.eu/themes/water/interactive/bathing/state-of-bathing-waters> [accessed 17 April 2017].
- Folkhälsomyndigheten. 2016. *Vibrioinfektioner* [in Swedish]. <https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/sjukdomsstatistik/vibrioinfektioner/> [accessed 17 April 2017].
- Frank C, Littman M, Alpers K, Hallauer J. 2006. *Vibrio vulnificus* wound infections after contact with the Baltic Sea, Germany. *Euro Surveill* 11:E060817.060811, PMID: 16966781.
- González-Escalona N, Cachicas V, Acevedo C, Rioseco ML, Vergara JA, Cabello F, et al. 2005. *Vibrio parahaemolyticus* diarrhea, Chile, 1998 and 2004. *Emerging Infect Dis* 11(1):129–131, PMID: 15705337, <https://doi.org/10.3201/eid1101.040762>.
- Heng SP, Letchumanan V, Deng CY, Ab Mutalib NS, Khan TM, Chuah LH, et al. 2017. *Vibrio vulnificus*: an environmental and clinical burden. *Front Microbiol* 8:997, PMID: 28620366, <https://doi.org/10.3389/fmicb.2017.00997>.
- Heymann DL, ed. 2008. *Control of Communicable Diseases Manual*. Washington, DC: American Public Health Association.
- Jacobs J, Moore SK, Kunkel KE, Sun L. 2015. A framework for examining climate-driven changes to the seasonality and geographical range of coastal pathogens and harmful algae. *Clim Risk Manag* 8:16–27, <https://doi.org/10.1016/j.crm.2015.03.002>.
- Johnson CN, Bowers JC, Griffith KJ, Molina V, Clostio RW, Pei S, et al. 2012. Ecology of *Vibrio parahaemolyticus* and *Vibrio vulnificus* in the coastal and estuarine waters of Louisiana, Maryland, Mississippi, and Washington (United States). *Appl Environ Microbiol* 78(20):7249–7257, PMID: 22865080, <https://doi.org/10.1128/AEM.01296-12>.
- Julie D, Solen L, Antoine V, Jaufrey C, Annick D, Dominique HH. 2010. Ecology of pathogenic and non-pathogenic *Vibrio parahaemolyticus* on the French Atlantic coast. Effects of temperature, salinity, turbidity and chlorophyll A. *Environ Microbiol* 12(4):929–937, PMID: 20100246, <https://doi.org/10.1111/j.1462-2920.2009.02136.x>.
- Kaspar CW, Tamplin ML. 1993. Effects of temperature and salinity on the survival of *Vibrio vulnificus* in seawater and shellfish. *Appl Environ Microbiol* 59(8):2425–2429, PMID: 8368832.
- Le Roux F, Wegner KM, Baker-Austin C, Vezzulli L, Osorio CR, Amaro C, et al. 2015. The emergence of *Vibrio* pathogens in Europe: ecology, evolution, and pathogenesis (Paris, 11–12th March 2015). *Front Microbiol* 6:830, PMID: 26322036, <https://doi.org/10.3389/fmicb.2015.00830>.
- Letchumanan V, Chan KG, Lee LH. 2014. *Vibrio parahaemolyticus*: a review on the pathogenesis, prevalence, and advance molecular identification techniques. *Front Microbiol* 5:705, PMID: 25566219, <https://doi.org/10.3389/fmicb.2014.00705>.
- Levy S. 2015. Warming trend: how climate shapes *Vibrio* ecology. *Environ Health Perspect* 123(4):A82–A89, PMID: 25831488, <https://doi.org/10.1289/ehp.123-A82>.
- Lindgren E, Andersson Y, Suk JE, Sudre B, Semenza JC. 2012. Public health. Monitoring EU emerging infectious disease risk due to climate change. *Science* 336(6080):418–419, PMID: 22539705, <https://doi.org/10.1126/science.1215735>.
- Lukinmaa S, Mattila K, Lehtinen V, Hakkinen M, Koskela M, Siitonen A. 2006. Territorial waters of the Baltic Sea as a source of infections caused by *Vibrio cholerae* non-O1, non-O139: report of 3 hospitalized cases. *Diagn Microbiol Infect Dis* 54(1):1–6, PMID: 16368474, <https://doi.org/10.1016/j.diagmicrobio.2005.06.020>.
- Martinez-Urtaza J, Baker-Austin C, Jones JL, Newton AE, Gonzalez-Aviles GD, DePaola A. 2013. Spread of Pacific Northwest *Vibrio parahaemolyticus* strain. *N Engl J Med* 369(16):1573–1574, PMID: 24131194, <https://doi.org/10.1056/NEJMc1305535>.
- Martinez-Urtaza J, Huapaya B, Gavilan RG, Blanco-Abad V, Ansedo-Bermejo J, Cadarso-Suarez C, et al. 2008. Emergence of asiatic *Vibrio* diseases in South America in phase with El Niño. *Epidemiology* 19(6):829–837, PMID: 18854707, <https://doi.org/10.1097/EDE.0b013e3181883d43>.
- McLaughlin JB, DePaola A, Bopp CA, Martinek KA, Napolilli NP, Allison CG, et al. 2005. Outbreak of *Vibrio parahaemolyticus* gastroenteritis associated with Alaskan oysters. *N Engl J Med* 353(14):1463–1470, PMID: 16207848, <https://doi.org/10.1056/NEJMoa051594>.
- Motes ML, DePaola A, Cook DW, Veazey JE, Hunsucker JC, Garthright WE, et al. 1998. Influence of water temperature and salinity on *Vibrio vulnificus* in northern Gulf and Atlantic Coast oysters (*Crassostrea virginica*). *Appl Environ Microbiol* 64(4):1459–1465, PMID: 9546182.
- Newton AE, Garrett N, Stroika SG, Halpin JL, Turnsek M, Mody RK. 2014. Increase in *Vibrioparahaemolyticus* infections associated with consumption of Atlantic coast shellfish—2013. *MMWR Morb Mortal Wkly Rep* 63(15):335–336, PMID: 24739344.
- Nichols GL, Andersson Y, Lindgren E, Devaux I, Semenza JC. 2014. European monitoring systems and data for assessing environmental and climate impacts on human infectious diseases. *Int J Environ Res Public Health* 11(4):3894–3936, PMID: 24722542, <https://doi.org/10.3390/ijerph110403894>.
- NOAA (National Oceanic and Atmospheric Administration). 2016. NOAA Optimum Interpolation (OI) SST v2. <http://www.esrl.noaa.gov/psd/data/gridded/tables/sst.html> [accessed 17 April 2017].
- Odeyemi OA. 2016. Incidence and prevalence of *Vibrio parahaemolyticus* in sea-food: a systematic review and meta-analysis. *Springerplus* 5:464, PMID: 27119068, <https://doi.org/10.1186/s40064-016-2115-7>.
- Oliver JD. 2005. Wound infections caused by *Vibrio vulnificus* and other marine bacteria. *Epidemiol Infect* 133(3):383–391, PMID: 15962544, <https://doi.org/10.1017/S0950268805003894>.
- Pfeffer CS, Hite MF, Oliver JD. 2003. Ecology of *Vibrio vulnificus* in estuarine waters of eastern North Carolina. *Appl Environ Microbiol* 69(6):3526–3531, PMID: 12788759, <https://doi.org/10.1128/AEM.69.6.3526-3531.2003>.
- Ruppert J, Panzig B, Guertler L, Hinz P, Schwesinger G, Felix SB, et al. 2004. Two cases of severe sepsis due to *Vibrio vulnificus* wound infection acquired in the Baltic Sea. *Eur J Clin Microbiol Infect Dis* 23(12):912–915, PMID: 15599654, <https://doi.org/10.1007/s10096-004-1241-2>.
- Semenza JC. 2015. Prototype early warning systems for vector-borne diseases in Europe. *Int J Environ Res Public Health* 12(6):6333–6351, PMID: 26042370, <https://doi.org/10.3390/ijerph120606333>.
- Semenza JC, Herbst S, Rechenburg A, Suk JE, Höser C, Schreiber C, et al. 2012. Climate change impact assessment of food- and waterborne diseases. *Crit Rev Environ Sci Technol* 42(8):857–890, PMID: 24808720, <https://doi.org/10.1080/10643389.2010.534706>.
- Semenza JC, Lindgren E, Balkanyi L, Espinosa L, Almqvist MS, Penttinen P, et al. 2016. Determinants and drivers of infectious disease threat events in Europe. *Emerging Infect Dis* 22(4):581–589, PMID: 26982104, <https://doi.org/10.3201/eid2204>.
- Semenza JC, Menne B. 2009. Climate change and infectious diseases in Europe. *Lancet Infect Dis* 9(6):365–375, PMID: 19467476, [https://doi.org/10.1016/S1473-3099\(09\)70104-5](https://doi.org/10.1016/S1473-3099(09)70104-5).
- Semenza JC, Sudre B, Oni T, Suk JE, Giesecke J. 2013. Linking environmental drivers to infectious diseases: the European Environment and Epidemiology Network. *PLoS Negl Trop Dis* 7(7):e2323, PMID: 23936561, <https://doi.org/10.1371/journal.pntd.0002323>.

- Swedish Code of Statutes. 2004. Swedish Communicable Diseases Act [in Swedish]. https://www.riksdagen.se/sv/dokument-lagar/dokument/svensk-forfattningssamling/smittskyddslag-2004168_sfs-2004-168 [accessed 17 April 2017].
- Tena D, Arias M, Alvarez BT, Mauleón C, Jiménez MP, Bisquert J. 2010. Fulminant necrotizing fasciitis due to *Vibrio parahaemolyticus*. J Med Microbiol 59(pt 2):235–238, PMID: [19797463](#), <https://doi.org/10.1099/jmm.0.014654-0>.
- Torres L, Escobar S, López AI, Marco ML, Pobo V. 2002. Wound infection due to *Vibrio vulnificus* in Spain. Eur J Clin Microbiol Infect Dis 21(7):537–538, PMID: [12172745](#), <https://doi.org/10.1007/s10096-002-0767-4>.
- Vezzulli L, Colwell RR, Pruzzo C. 2013. Ocean warming and spread of pathogenic vibrios in the aquatic environment. Microb Ecol 65(4):817–825, PMID: [23280498](#), <https://doi.org/10.1007/s00248-012-0163-2>.
- Westrich JR, Ebling AM, Landing WM, Joyner JL, Kemp KM, Griffin DW, et al. 2016. Saharan dust nutrients promote *Vibrio* bloom formation in marine surface waters. Proc Natl Acad Sci U S A 113(21):5964–5969, PMID: [27162369](#), <https://doi.org/10.1073/pnas.1518080113>.
- Whitaker WB, Parent MA, Naughton LM, Richards GP, Blumerman SL, Boyd EF. 2010. Modulation of responses of *Vibrio parahaemolyticus* O3:K6 to pH and temperature stresses by growth at different salt concentrations. Appl Environ Microbiol 76(14):4720–4729, PMID: [20472729](#), <https://doi.org/10.1128/AEM.00474-10>.
- Yeung PS, Hayes MC, DePaola A, Kaysner CA, Kornstein L, Boor KJ. 2002. Comparative phenotypic, molecular, and virulence characterization of *Vibrio parahaemolyticus* O3:K6 isolates. Appl Environ Microbiol 68(6):2901–2909, PMID: [12039748](#), <https://doi.org/10.1128/AEM.68.6.2901-2909.2002>.